510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k052407

B. Purpose for Submission:
New Device

C. Measurand:
Thyroid peroxidase autoantibodies (Anti-TPO), IgG

D. Type of Test:
Quantitative Chemiluminescent Microparticle Immunoassay

E. Applicant:
Fisher Diagnostics

F. Proprietary and Established Names:
Architect® Anti-TPO Immunoassay Reagents
Architect® Anti-TPO Calibrators and controls

G. Regulatory Information:

1. Regulation section:
   21 CFR 866.5870, Thyroid Autoantibody Immunological Test System
   21 CFR 862.1660, Quality Control Material (Assayed and Unassayed)
   21 CFR 862.1150, Calibrator
2. Classification:
   Class II
3. Product code:
   JZO - Thyroid Antibody Test System
   JJX - Single (specified) Analyte Control (Assayed and Unassayed)
   JIT - Calibrator, Secondary
4. Panel:
   Immunology 82
   Clinical chemistry 75

H. Intended Use:

1. Intended use(s):
   Architect® Anti-TPO is a chemiluminescent microparticle Immunoassay (CMIA) for the quantitative determination of the IgG class of thyroid peroxidase autoantibodies (anti-TPO) in human serum and plasma (EDTA and Heparin) on the Architect® *i* System. The Architect® Anti-TPO assay is intended for use as an aid in the diagnosis of autoimmune thyroid disease.

   The Architect®Anti-TPO Calibrators are for the calibration of the Architect® *i* System when used for the quantitative determination of IgG class of thyroid peroxidase autoantibodies (anti-TPO) in human serum and plasma. The Architect® Anti-TPO controls are for the estimation of test precision and the detection systematic analytical deviations of the Architect® *i* System when used for the quantitative determination of IgG class of thyroid peroxidase autoantibodies (ant-TPO) in human serum and plasma.
2. Indication(s) for use:

Same as intended use.

3. Special conditions for use statement(s):
   For prescription use only.
4. Special instrument requirements:
   Architect *i* System (Architect® *i*2000 and Architect *i* 200SR).

I. Device Description:

The device consists of (a) TPO coated paramagnetic particles, (b) sample diluent MES buffer with protein-goat, (c) Anti-human IgG (mouse monoclonal) acridinium labeled conjugate, (d) wash buffer, (e) Architect *i* pre-trigger and trigger solutions,(f) calibrators, (g) controls and (h) a CD-ROM containing the assay files to be installed in the Architect *i* System.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Abbott's AxSYM anti-Thyroid Microparticle Enzyme Immunoassay
2. Predicate 510(k) number(s):
   k020348
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended use	aid in the diagnosis of autoimmune thyroid disease	Same
Assay format	Quantitative	Same
Number of Calibrators	6 levels (A-F)	same
Calibrator Range concentrations	0.0-1000 IU/mL	same
Standardization material	NIBSC MRC 66/387 Anti-Thyroid microsome serum standard	Same
Control component	Human plasma	same

Differences		
Item	Device	Predicate
Thyroid peroxidase - microparticle coating	Recombinant	From human thyroid glands
Conjugate	Mouse anti-human IgG (monoclonal) acridinium labeled in MES buffer	Goat anti-human IgG alkaline phosphate-in TRIS buffer
Control concentrations and range	Negative 0.0IU/mL Range ≤ 2.15 IU/mL Positive 75 IU/mL Range 45-105 IU/mL	Negative 0.0 IU/mL Range ≤ 12.0 IU/mL Positive 75 IU/mL Range 40-110 IU/mL
Assay diluent	MES buffer	TRIS buffer
Assay method	Chemiluminescent microparticle (CMIA)	Microparticle enzyme (MEIA)
Analyzer	Architect *i* System	AxSYM System

K. Standard/Guidance Document Referenced (if applicable):

CLSI (NCCLS) EP5-A, EP6-A, EP7-A, EP17-A.

L. Test Principle:

Chemiluminescent microparticle immunoassay (CMIA) referred as Chemiflex. It is a two step assay. In the first step sample and assay diluent (MES buffer) and TPO coated paramagnetic particles are mixed and incubated. Anti-TPO in the sample binds to the microparticles. After a wash step anti-human acridinium labeled conjugate is added in the second step. Following an incubation and wash cycle pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units(RLU). A direct relationship exists between the amount of anti-TPO in the sample and the RLUs detected by the Architect *i* system optics.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision studies were performed using Positive Control and 3 human panels (serum pools with low, medium and high concentrations), 3 lots of reagents in replicates of two at 2 separate times per day for 20 days on 3 instruments (according to CLSI EP5-A).

ARCHITECT Anti-TPO assay is designed to have an assay precision of ≤ 10% total CV for samples ≥ 5.61 IU/mL. Each reagent lot used a single calibration curve throughout the study. Data from this study are summarized in the following table.*

Sample	Instrument	Reagent Lot	n	Mean Conc. (IU/mL)	Within Run		Total	
					SD	% CV	SD	% CV
Positive Control	1	A	80	74.85	2.11	2.8	2.16	2.9
		B	80	74.20	1.89	2.6	2.04	2.7
		C	80	74.63	2.01	2.7	2.17	2.9
	2	A	80	77.42	2.11	2.7	3.25	4.2
		B	80	75.32	1.92	2.5	2.54	3.4
		C	80	74.59	1.73	2.3	2.57	3.4
	3	A	80	75.41	2.13	2.8	2.52	3.3
		B	80	75.48	1.90	2.5	2.13	2.8
		C	80	76.66	2.42	3.2	2.87	3.7
Panel 1	1	A	80	1.57	0.08	4.8	0.10	6.5
		B	80	1.46	0.06	3.8	0.09	5.8
		C	80	1.64	0.09	5.6	0.10	6.1
	2	A	80	1.60	0.09	5.3	0.12	7.6
		B	80	1.53	0.06	3.9	0.11	7.2
		C	80	1.52	0.10	6.7	0.12	7.7
	3	A	80	1.47	0.08	5.3	0.11	7.8
		B	80	1.47	0.07	4.7	0.13	8.5
		C	80	1.52	0.14	9.5	0.15	9.8

Sample	Instrument	Reagent Lot	n	Mean Conc. (IU/mL)	Within Run		Total	
					SD	% CV	SD	% CV
Panel 2	1	A	80	20.98	0.65	3.1	0.76	3.6
		B	80	21.14	0.61	2.9	0.66	3.1
		C	80	21.51	0.71	3.3	0.75	3.5
	2	A	80	21.27	0.61	2.9	0.98	4.6
		B	80	21.62	0.66	3.0	0.90	4.2
		C	80	20.82	0.67	3.2	0.85	4.1
	3	A	80	21.00	0.73	3.5	0.86	4.1
		B	80	21.77	0.60	2.7	0.84	3.8
		C	80	21.24	0.70	3.3	0.89	4.2
Panel 3	1	A	80	214.78	5.14	2.4	6.48	3.0
		B	80	221.79	4.73	2.1	5.82	2.6
		C	80	216.71	5.36	2.5	6.36	2.9
	2	A	80	219.32	4.41	2.0	8.61	3.9
		B	80	224.54	4.04	1.8	13.37	6.0
		C	80	218.73	5.76	2.6	13.18	6.0
	3	A	80	212.91	6.11	2.9	6.84	3.2
		B	80	225.46	5.15	2.3	5.67	2.5
		C	80	228.17	5.80	2.5	7.09	3.1

b. Linearity/assay reportable range:

The assay was shown to be linear from 3.0 to 1000.0 IU/mL by the following study: three high sample pools (1000, 300, and 30 IU/mL) were combined with a low pool calibrator A to provide 9 test points. All test points were analyzed in replicates of 5 using a single reagent lot. Automated dilution was compared to a manual 1:2 dilution using 9 human specimens with anti-TPO levels that were greater than calibrator E (250 IU/mL). The manual dilution was done with Anti-TPO calibrator A. Summary of results is shown in the following table.

Sample ID	Automated Dilution (IU/mL)	Manual Dilution (IU/mL)	% Recovery
1	861.25	859.27	100.2
2	684.49	703.64	97.3
3	844.36	847.62	99.6
4	724.55	757.09	95.7
5	709.46	688.49	103.1
6	1105.65	1106.18	100.0
7	948.43	931.80	101.8
8	840.77	851.72	98.7
9	966.48	998.44	96.8

High dose hook – Ten samples with anti-TPO concentrations of 3458 IU/mL to 17815 IU/mL were analyzed and results were reported as >1000 IU/mL. No high dose

hook effect was observed.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
The anti-TPO reference calibrator is traceable to the NIBSC 66/387 reference preparation. The anti-TPO reference calibrators are produced from the NIBSC 66/387 reference preparation with individual levels at 30.0, 15.0, 5.0, 1.5, 0.75, and 0.0 IU/mL. The proper weight fractions of the stock concentrate and calibrator diluent were mixed to form the individual levels anti-TPO master calibrator at 0.00, 5.0, 20.0, 62.5, 250.0, and 1000.0 IU/mL. The calibrators and controls are manufactured from human anti-TPO positive plasma pools.

Stability – Stability was established based on accelerated and real time studies on three lots of Calibrators at various temperatures (5, 25, 30, 35, -20 and -50° C). Stability test results and graphs are in the submission. The results indicate storage stability for 12 months when stored at -10°C. On-board stability is 30 days. Stability of reagents stored at 2-8° is shown as 9 months.

d. *Limit of Blank:*
Limit of Blank was tested using 10 replicates of calibrator A and 4 replicates of calibrator B per run. The acceptance criterion was ≤ 1.0 IU/mL. 36 total runs were made across 3 instruments (*i* 2000) using 3 different reagent lots. The Limit of Blank was calculated as mean of all calculations plus 2 SDs for type 1 error of 2.5 %. The Limit of Blank is 0.159 IU/mL for all 3 lots.

e. *Analytical specificity:*
Interference from elevated levels of bilirubin (20mg/dl), hemoglobin (1000 mg/dl) triglycerides (1000mg/dl) and total protein 10g/dl) were tested. A study was performed based on CLSI EP7-A. Specimens with anti-TPO levels between 45.07 and 361.64 IU/mL were used. Specimens were spiked between 133.44 and 568.78 IU/mL. The average interference observed ranged from -3.6% to + 3.7% (within ≤15% acceptable range).

f. *Assay cut-off:*
Values greater than 5.6 IU/mL are considered positive.

2. Comparison studies:

a. *Method comparison with predicate device:*
The performance of the Architect Anti-TPO was compared to AxSYM Anti-TPO assay. A total of 500 specimens (236 samples from healthy individuals and 264 samples from patients with autoimmune thyroid disease- 125 Graves' disease and 139 Hashimoto's Disease) were evaluated. Specimens were tested in replicates of one using the Architect Anti-TPO assay with three reagent lots. 446 samples were < 1000 IU/mL. The remaining 54 samples were not included in the correlation since their anti-TPO concentrations were greater than the assay range (> 1000 IU/mL). Data from this study are summarized in the following table.

ARCHITECT Anti-TPO	AxSYM Anti-TPO		
	Negative	Positive	Total
Negative	242	32	274
Positive	5	221	226
Total	247	253	500

Negative Agreement=98.0% (242/247) with 95% CI: 95.3% to 99.3%

Positive Agreement= 87.4% (221/253) with 95% CI: 82.6% to 91.2%

Total Agreement= 92.6 %

Sample Range (ARCHITECT) = 0.0 to 27430.8 IU/mL
Sample Range (AxSYM Anti-TPO) = 1.5 to 50390 IU/mL

Linear Regression Analysis				
Specimen Type	n	Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient
Autoimmune Thyroid Disease	211	1.198 (1.138 to 1.259)	15.34 (-3.25 to 33.93)	0.937
Apparently Healthy Individuals	235	0.924 (0.909 to 0.938)	-3.34 (-4.35 to -2.34)	0.993

b. Matrix comparison:

Twenty donors were evaluated in each of the nine tubes – serum separator tube plus vs. serum, sodium heparin glass vs. serum, sodium heparin plastic vs. serum, lithium heparin glass vs. serum, lithium plastic vs. serum, plasma separator lithium heparin glass vs. serum, plasma separator lithium heparin plastic vs. serum, EDTA glass vs. serum and EDTA plastic vs. serum. For each donor, samples from each tube type were assayed in replicates of five. Samples from two donors with anti-TPO values greater than the assay range were excluded from the analysis. The mean percentage interference ranged from 1.16 to 1.8%. Linear regression analysis was also performed and results are summarized below.

Serum separator tube plus vs. serum, $y = 1.0178x – 2.7939$, $R^2 = 0.9995$
Sodium Heparin glass vs. serum, $y = 1.0036x + 1.1448$, $R^2 = 0.9995$
Sodium Heparin plastic vs. serum, $y = 1.012x -1.3539$, $R^2 = 0.9995$
Lithium Heparin glass vs. serum, $y = 1.0097x – 0.8132$, $R^2 = 0.9996$
Lithium Heparin plastic vs. serum, $y = 1.0163x – 2.0565$, $R^2 = 0.9995$
Plastic separator Lithium Heparin glass vs. serum, $y = 1.007x – 0.964$, $R^2 = 0.9996$
Plastic separator Lithium Heparin plastic vs. serum, $y = 1.0104x – 1.994$, $R^2 = 0.9996$
EDTA glass vs. serum, $y = 0.997x-1.3241$, $R^2 = 0.9998$
EDTA plastic vs. serum, $y = 1.0088x – 1.2826$, $R^2 = 0.9993$

3. Clinical studies:

a. Clinical Sensitivity:

Clinical sensitivity was evaluated by testing 139 clinically defined Hashimoto's Thyroiditis and 125 Grave's Disease specimens. Anti-TPO levels ≥ 5.6 IU/mL is considered positive for Architect assay and ≥12 IU/mL for comparison assay.
The samples used in the method comparison study were from multiple collection sites

and tested at the sponsor's facility at two different timings noted as study 1 and study 2. The results are summarized below:

ARCHITECT Anti-TPO						
Hashimoto's Thyroiditis				Graves' Disease		
Study #	n	No. of Positive	% Positive (95% CI)	n	No. of Positive	% Positive (95% CI)
1	89	57	64.0 (53.2 to 73.9)	75	69	92.0 (83.4 to 97.0)
2	50	37	74.0 (59.7 to 85.4)	50	50	100.0 (92.9 to 100.0)
Total	139	94	67.6 (59.2 to 75.3)	125	119	95.2 (89.8 to 98.2)

Comparison Assay-AxSYM Anti-TPO						
1	89	76	85.4 (76.3 to 92.0)	75	71	94.7 (86.9 to 98.5)
2	50	47	94.0 (83.5 to 98.7)	50	50	100.0 (92.9 to 100.0)
Total	139	123	88.5 (82.0 to 93.3)	125	121	96.8 (92.0 to 99.1)

There was a decrease in clinical sensitivity for Hashimoto's Thyroiditis of 20.9%.

b. Clinical specificity:
Besides Grave's and Hashimoto's disease no other autoimmune diseases were tested.

c. Other clinical supportive data (when a and b are not applicable):
None

4. Clinical cut-off:
5.61 IU/mL
5. Expected values/Reference range:
Human serum specimens were collected from a population of 236 apparently healthy individuals. All specimens had TSH values within the normal reference range. Of this study population, 9 specimens delivered positive results on a commercially available anti-TPO assay device and were excluded from further normal range analysis. The 97.5 percentile concentration of the remaining population was 5.61 IU/mL. In this study population, the normal range is < 5.61 IU/mL. A total of 97.8% (222/227) of the population had values within this normal range.

N. Proposed Labeling:
The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10

O. Conclusion:
The submitted information in this premarket notification is complete and supports a substantial equivalence decision.